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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/804,938	03/19/2004	John Link	10031165-1	8132

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EXAMINER	
CROW, ROBERT THOMAS	
ART UNIT	**PAPER NUMBER**
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/804,938	LINK ET AL.	
	Examiner	Art Unit	
	Robert T. Crow	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *15 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,20 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15 and 20-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 15 December in which claims 1-2 were amended, no claims were canceled, and new claims 20-21 were added. All of the amendments have been thoroughly reviewed and entered.

The objection to the Petition for color drawing listed in the previous Office Action is maintained because Applicant has not amended the specification so that the paragraph in the Specification regarding color drawings is the first paragraph of the brief description of the drawings.

The previous rejections under 35 U.S.C. 112, second paragraph, not reiterated below are withdrawn in view of the amendments.

The previous rejections under 35 U.S.C. 103(a) not reiterated below are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed and are addressed following the rejections necessitated by the amendments.

Claims 1-15 and 20-21 are under prosecution.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 2-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 2-6 and are indefinite in claims 2-5, which recite the limitations "BTS" and "MMM" in lines 2-3 of claim 2, line 1 of claim 3, lines 1-2 of claim 4, and lines 4, and lines 1-2 of 5, because they are acronyms, the

meanings of which may change over time. It is suggested that each of the claims be amended to recite each of the polymers in each instance by their respective full names.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1, 10-15, and 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sambrook et al (Molecular Cloning, A Laboratory Manual, 2nd ed., Cold Spring Harbor Laboratory Press, NY, pp. 7.12-7.15 and pp. 7.23-7.29 (1989)) in view of Wang et al (U.S. Patent No 5,219,727, issued 15 June 1993).

Regarding claims 1, 10-15, 20-21, Sambrook et al teach a method of preparing an RNA sample substantially free of contaminants. In a single exemplary embodiment, Sambrook et al teach preparation of an RNA sample (pages 7.23), followed by addition of the organic solvent ethanol (i.e., claim 14) to the

RNA sample (page 7.25, step 19). Sambrook et al further teach the RNA preparation is subjected to removal of DNA by the enzyme DNAse I (i.e., claim 20), which is added to the RNA sample preparation ("note" on page 7.25, and page 7.14, steps 10-17). Sambrook et al further teach addition of a wash buffer (i.e., solution) comprising the chaotropic agent guanidine hydrochloride (i.e., claim 21; page 7.24, step 6). Sambrook et al further teach contacting an RNA isolation membrane column with said RNA-containing precipitate; namely, performing chromatography on the RNA (page 7.15, paragraph ii). The chromatography is performed in a column comprising a membrane; namely, a Dispocolumn comprising a oligo(dT) cellulose and a glass wool plug (page 7.26, step 2). The glass wool of Sambrook et al is interpreted as a membrane because a "wool" comprises a multi-fiber interwoven structure (i.e., a membrane) having spaces between individual fibers (i.e., pores). Because the column has oligo(dT) cellulose, the column is an RNA isolation column because polyadenlyated (i.e., polyA+) RNAs are isolated by the column (i.e., claim 15). The RNA is then eluted from the membrane column (page 7.29).

Claims 10-13 are drawn to RNA that is from about 55-65, 65-75, 75-85, and 85 to $\geq$95% pure. The claims do not define what the RNA is purified from so as to define the purity. Because Sambrook et al teach the RNA is separated and purified (page 7.15, paragraph ii), the RNA of Sambrook et al is encompassed by the broadly claimed purity of instant claims 10-13.

It is noted that the claim appears to be drawn to a method wherein both the addition of the DNAse enzymes and the addition of the chaotropic salt occur while the RNA sample is still on the column. While Sambrook et al does not explicitly teach the DNAse and the chaotropic salt are added to the RNA on the column, the courts have held that selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results (*In re Burhans*, 154 F.2d 690, 69 USPQ 330 (CCPA 1946)). See MPEP 2144.04 IV.C.

Sambrook et al do not teach the RNA is cRNA.

However, Wang et al teach a method of preparing a cRNA sample substantially free of contaminants using an RNA isolation column in the form of selective elution of cRNA a QIAGEN-tip spin

column and oligo(dT) chromatography (column 13, Example 1). Wang et al further teach that a single cRNA has the added advantage of allowing quantitation of mRNA as well as acting as a internal standard template for reverse transcription reactions (column 8, line 65-column 9, line 23).

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method of preparing an RNA sample substantially free of contaminants as taught by Sambrook et al to prepare cRNA as taught by Wang et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in a method of preparing a cRNA sample substantially free of contaminants having the added advantage of purifying an RNA that has the added advantage of allowing quantitation of mRNA as well as acting as a internal standard template for reverse transcription reactions as explicitly taught by Wang et al (column 8, line 65-column 9, line 23).

7. Claims 2-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sambrook et al (Molecular Cloning, A Laboratory Manual, 2nd ed., Cold Spring Harbor Laboratory Press, NY, pp. 7.12-7.15 and pp. 7.23-7.29 (1989)) in view of Wang et al (U.S. Patent No 5,219,727, issued 15 June 1993) as applied to claim 1 above, and further in view of Wang et al (U.S. Patent No. 5,906,742, issued 25 May 1999) as evidenced by Pall Life Sciences (Bulletin #FAM-1050-C, Pall Corporation, Filterite Advanced Materials Division, San Diego, CA, 2002).

It is noted that while Bulletin #FAM-1050-C, from the Pall Corporation, Filterite Advanced Materials Division of San Diego, CA, is a new piece of art that has been placed on the record, it is provided only as evidence that the MMM membranes of the Pall corporation were constructed of PVP and polysulfone in 2002.

Regarding claims 2-4, the method of claim 1 is discussed on pages 3-6 above. The Specification teaches that MMM membranes are available from Pall Life Sciences (page 15, paragraph 0061). Bulletin

#FAM-1050-C from Pall Life Sciences defines MMM membranes as asymmetric membranes composed of polysulfone and PVP.

While Sambrook et al teach the column comprises a membrane (column 6, lines 52-55), Sambrook et al and Wang et al are silent with respect to MMM membranes.

However, Wang et al '742 teach the use of solid phases in the form of asymmetric microfiltration membrane materials (Abstract, lines 1-2) comprising PVP (i.e., polyvinylpyrrolidone) co-cast with polysulfone (Abstract, lines 7-11) for filtering biological samples (e.g., whole blood; Abstract, lines 11-12) with the added advantage that the membranes are highly useful in the quick detection of components contained in liquid samples (Abstract, lines 14-16).

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method comprising a membrane as taught by Sambrook et al and Wang et al with the membrane as taught by Wang et al '742 with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because such a modification would have resulted a method of preparing a cRNA sample substantially free of contaminants having the added advantage of allowing the quick detection of components contained in liquid samples as explicitly taught by Wang et al (Abstract, lines 14-16).

Regarding claims 5-6, the method of claim 3 is discussed above. Wang et al also teach the MMM membrane has a pore size ranging from about 30 μm to about 40 μm on an upper side, and wherein said MMM membrane has a pore size of about 0.8 μm on a lowers side; namely, the membrane has a pore size around 1.0 μm and opens to about 50 μm (column 10, line 59- column 11, line 1). In addition, the courts have stated where the claimed ranges "overlap or lie inside the ranged disclosed by the prior art" and even when the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have similar properties, a *prima facie* case of obviousness exists (see *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990); *Titanium Metals Corp. of America v. Banner*, 778 F2d 775. 227 USPQ 773 (Fed. Cir. 1985) (see

MPEP 2144.05.01). Therefore, the claimed range of a pore size ranging from about 30 μm to about 40 μm on an upper side, and wherein said MMM membrane has a pore size of about 0.8 μm on a lower side would have been obvious under the pore size around 1.0 μm that opens to about 50 μm as taught by Wang et al.

8. Claims 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sambrook et al (Molecular Cloning, A Laboratory Manual, 2nd ed., Cold Spring Harbor Laboratory Press, NY, pp. 7.12-7.15 and pp. 7.23-7.29 (1989)) in view of Wang et al (U.S. Patent No 5,219,727, issued 15 June 1993) as applied to claim 1 above, and further in view of Waggoner (U.S. Patent No. 5,627,027, issued 6 May 1997).

Regarding claims 7-9, the method of claim 1 is discussed on pages 3-6 above. While Wang teaches labeled amplified DNA (column 11, lines 59-67), neither Sambrook et al nor Wang et al teach labeled RNA.

However, Waggoner teaches the labeling of RNA using fluorescent cyanine dyes (i.e., claims 8-9; Abstract) with the added advantage that cyanine-labeled nucleic acids help reduce non-specific binding to irrelevant components in a mixture (Abstract, last five lines).

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method as taught by Sambrook et al in view of Wang et al with the label as taught by Waggoner with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because such a modification would have resulted a method of preparing a cRNA sample substantially free of contaminants having the added advantage of reduction of non-specific binding to irrelevant components in a mixture as explicitly taught by Waggoner (Abstract, last five lines).

Response to Arguments

9. Applicant's arguments with respect to the previous rejections of the claims have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

10. No claim is allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

12. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571) 272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

RAM R. SHUKLA, PH.D.
SUPERVISORY PATENT EXAMINER

Robert T. Crow
Examiner
Art Unit 1634